REMARKS

A. Regarding the Amendments

Claims 1-5 and 10-14 have been amended merely to claim the invention with greater precision and particularity. The specification has been amended to correct typographical and clerical errors. Claim 16 has been added. Accordingly, claims 1-16 are pending of which claims 10-15 have been withdrawn from consideration. Therefore, claims 1-9 and 16 are currently under examination. For the rejoinder procedure purpose under MPEP 821.04, in order to expedite prosecution, claims 10-14 now withdrawn from consideration have been amended, as per 37 CFR § 121(c)(2) to include all the limitations of the product claims.

No new matter has been introduced by the claims amendments or by the specification amendments. In particular, the subject matter claimed in the newly added claim 16 is disclosed in the originally filed application (see, page 6, lines 16-21, and original claim 9). The concept of the pharmaceutical preparations as an adjuvant of claim 1 has been demonstrated in Examples 7 through 14.

B. The Restriction Requirement

The Applicants acknowledge the fact that the restriction and election requirements have been made final (item 1 on page 2 of the Office Action).

C. Objections to the Specification

The Examiner objected to the specification (item 2, page 2 of the Office Action). Appropriate changes have been made to correct the typographical and printing errors on pages 7, 11, and 20, as required by the Examiner. In addition, other similar corrections have been made throughout the specification. Accordingly, withdrawal of the objection to the specification is respectfully requested.

D. Objections to Claims

The Examiner objected to claims 2-9 (item 3, page 2 of the Office Action) due to alleged lack of antecedent basis. Claim 2 has been amended to delete "directly linked to the presenegenin skeleton at position 28." It is therefore submitted that the objections no longer apply. Accordingly, withdrawal of the objections to claims 2-9 is respectfully requested.

E. Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-9 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention (item 4 on page 3 of the Office Action). The rejection is respectfully traversed.

Specifically, the Examiner has objected to the use of the term "essentially comprises" in claim 1. Claim 1 has been amended and now recites "comprises" instead of "essentially comprises." Accordingly, withdrawal of the rejections and reconsideration are respectfully requested.

F. Rejection Under 35 U.S.C. § 112, First Paragraph

Claim 9 has been rejected under 35 U.S.C. § 112, first paragraph, as allegedly being non-enabled (item 5, pages 3-7 of the Office Action). The rejection is respectfully traversed.

More particularly, the Examiner has asserted that the specification does not enable vaccine preparations for *Helicobacter pylori*, enterohaemorrhagic *Escherichia coli* (EHEC), *Chlamydia*, *Mycoplasma*, *Plasmodium*, coccidium, and schistosome. The Examiner based his rejection on the allegation that there are no vaccines for the above-mentioned pathogens, and supported this allegation by citing to various references.

The Applicants respectfully disagree. The following references published before the present application have disclosed the development of various vaccines for above-mentioned pathogens, and/or demonstrated the prevention of diseases caused by these pathogens in at least mammals and/or poultry.

Helicobacter pylori (H. pylori)

The international publication of the international application numbers, WO 98/23288, WO 98/56412, WO 98/56815, WO 98/56816, WO 99/21959 and WO 99/49890, have disclosed a various vaccines for this pathogen.

i. Enterohaemorrhagic *Escherichia coli* (EHEC)

Weekly Epidemiological Record, Vol.74, No.14 (Apr 9, 1999) p105-111, entitled as "New frontiers in the development of vaccines against enterotoxinogenic (ETEC) and enterohaemorrhagic (EHEC) E.coli infections, Part II" has disclosed the development of the vaccines for this pathogen.

Table 1 on page 1085 of Nippon Rinsho, Vol.60, No.6 (2002) p.1083-1088, has summarized various vaccines for this pathogen with specific references (Nos.3 to 22 as listed on page 1087-1088), which were developed in 1990s and demonstrated to be applicable in at least in mouse, rat, rabbit and/or pig.

ii. *Chlamydia*

US Patents Nos. 5,840,297, 5,656, 271, 5,242,686, 4,271,146, and 4,267,170, and patent documents WO 97/06263, WO 98/28005, and WO 99/10005, have disclosed various vaccines for this pathogen.

iii. *Mycoplasma*

Haesebrouck et al, Veterinary Microbiology, Vol.100 (2004) p.255-268 describes that the vaccines for pigs to controle *Mycoplasma* hyponeumoniae infections has been available in 1990s (see page 263, lines 13-21 in left column, and from line 45 to line 2 in right column).

Maes et al, Vaccine, Vol.17 (1999) p.1024-1034 describes the effective vaccines against *Mycoplasma* hyponeumoniae infections in pigs.

iv. *Plasmodium*

US Patent Nos. 5,853,739, 5,720,959, and 5,229,110, and patent documents WO 97/26911 and WO 98/05355, have disclosed various vaccines for this pathogen.

v. *Coccidium*

Williams et al, Avian Pathology Vol.31 (2002) p.317-353 reviews various vaccines applicable for poultry against this pathogen, which have been commercialized from before 1990 (see, Table 1 on page 319).

Allen at al, Clinical Microbiology Reviews, Vol.15, No.1 (2002) p.58-65 reviews the development, available vaccines so far and effects of the vaccines to control of infection with Coccidium of poultry.

vi. Schistosomes

US Patent No. 5,730984 has disclosed various vaccine for this pathogen.

Accordingly, all the claims are clearly enabled, since, at the time of filing of the present application, a person having ordinary skill in the art would have known of the existence of vaccines for the above-mentioned pathogens, and could practice the present invention as described in the disclosure of the present application.

Furthermore, even if the Examiner's conclusion were correct with respect to the non-existence of vaccines for the above-mentioned pathogens, it could be correct only if the term "vaccine" is given the meaning provided by the Examiner. The Examiner's definition focuses on prevention a disease in the future by inducing a protective immune response in the present (see, Office Action, page 4, lines 11-15). However, this definition is too narrow and is not how the term "vaccine" is defined by the Applicants.

It is axiomatic that an applicant is his own lexicographer. See, e.g., *In re Paulsen*, 30 F.3d 1475, 1480, 31 USPQ 2d 1671, 1674 (Fed. Cir. 1994). An applicant is always allowed to use his own definitions of terms and special meanings , which may be different from common usage, so long as clear definition of such special meaning is provided by a specification. See,

e.g., *Intellicall, Inc. v. Phonometrics, Inc.*, 952 F.2d 1384, 1387-88, 21 USPQ 2d 1383, 1386 (Fed. Cir. 1992). Accordingly, the Applicants gave a special meaning to the term "vaccine" which includes a broad definition, and covers the preparations which are effective not only for "prevention," but also for "treatment" of the diseases (see, specification, page 11, lines 17-19). Clearly, the Applicants mean to include in definition of the "vaccine" the preparations that can be used for treatment of a disease in the situation when the disease has not been prevented.

Therefore, even if there were no "vaccines" in the narrow sense, that is, those effective for "prevention" *Helicobacter pylori*, enterohaemorrhagic *Escherichia coli* (EHEC), *Chlamydia*, *Mycoplasma*, *Plasmodium*, coccidium, and schistosome, the Examiner has provided no evidence showing that there are no such "vaccines" in the broad sense, that is, the preparations that can be used for treatment of these conditions.

Accordingly, it is submitted that the rejection under 35 U.S.C. § 112, first paragraph does not apply. Withdrawal of the rejection and reconsideration are respectfully requested.

G. Rejection Under 35 U.S.C. § 102 (b)

Claims 1-6 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Sakuma et al. (Chem. Pharm. Bull., 1981, 30(3):810-821) (item 6, pages 7-8 of the Office Action). This rejection is respectfully traversed. Hereinafter, this reference is referred to as "Sakuma II." The Applicants respectfully point out that the correct year of publication of this reference is 1982.

The legal standard for a valid rejection by anticipation is well established. A valid rejection of a claim for anticipation by a reference requires that the reference explicitly or inherently describe all of the elements, limitations, and relationships recited in the claim. It is submitted that Sakuma II fails to satisfy this standard.

Claim 1, as amended, recites "a sugar residue substituted with a trimethoxycinnamate residue," defining the structure of a saponin compound which composes the subject adjuvant. Sakuma II describes the structure of only onijisaponins A, B, and E. See, the title, the abstract,

and page 810, line 4 (following the abstract) in Sakuma II. Contrary to the Examiner's assertion (see, Office Action, page 8, lines 9-12), although Sakuma II does mention in passing that they reported the structure of the onjisaponins F and G in their previous paper, they do not describe the structure of onijispaonins F and G in the cited Sakuma II. Hereinafter, that previous paper by Sakuma et al (Chem. Pharm. Bull., 1981, 29(9):2431-2441) is referred to as "Sakuma I." The Applicants have previously provided the Examiner with a copy of Sakuma I (Document A3 in the Information Disclosure Statement filed on October 17, 2002. While Sakuma I describes the structure of onjisaponins F and G, the structures of the onjisaponins A, B and E have never been described.

The structure of onjisaponins A, B and E (described in Sakuma II), and F and G (described in Sakuma I) can be summarized as shown below, for the structure recited in the present claim 4.

	position 23	R1	R2	R3	R4	R5
Onjisaponin A	COOH	MC	Rha	Api	H	Gal
Onjisaponin B	COOH	MC	Rha	H	H	Gal
Onjisaponin E	COOH	TC	H	H	H	Gal
Onjisaponin F	COOH	TC	H	Api	Ara	H
Onjisaponin G	COOH	TC	H	Api	H	H

MC: (mono)methoxycinnamate group; TC: trimethoxycinnamate group; Rha: rhamnose residue; Api: apiose residue; Ara: arabinose residue; and Gal: galactose residue

A saponin compound recited in claim 1 includes onjisaponins E, F and G, and, due to the presence of the trimethoxycinnamate moiety, indeed excludes onjisaponins A and B.

Accordingly, neither Sakuma II nor Sakuma I describes the use of the onjisaponin compounds recited in claim 1. Both the Sakuma II and Sakuma I describe just a chemical determination of the structure of onjisaponins A, B and E (in Sakuma II), and onjisaponins F and G (in Sakuma I).

In view of the foregoing, claim 1 is patentably distinguishable over Sakuma et al (Sakuma II). Each of claims 2-6 depends on claim 1 and is considered patentable at least for the same reasons. Withdrawal of the rejection and reconsideration are respectfully requested.

H. Rejection Under 35 U.S.C. § 103 (a)

Claims 7-9 have been rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Sakuma et al. in view of Kensil (Critical Reviews in Therapeutic Drug Carrier Systems, 1996, 13(1/2):1-55 (item 7 on pages 8-10 of the Office Action). This rejection is respectfully traversed.

To establish a *prima facie* case of obviousness over a combination of references, the following three basic criteria must be met: (1) there must be some suggestion or motivation to combine the references as proposed by the Examiner; (2) there must be a reasonable expectation of success as a result of such combination; and (3) when all the references are combined, the combination must teach or suggest all of the claim limitations. The Applicants respectfully submits that none of the criteria has been satisfied in this case because the above-mentioned combinations of references fail to teach or suggest every limitation of claims 7- 9.

Kensil reference only reviews a structure-function relationship of a partially purified preparations, Quil A, extracted from a plant, *Quillaja saponaria*, and saponins QS-7, QS-17, QS-18 and QS-21 isolated from the partial Quil A preparations for an adjuvant activity (See Abstract and Background parts on page 1 and 2).

The saponins having a "quillaic acid" skeleton that have been described and reviewed in Kensil reference are completely different compounds from the saponins having a "presenegenin" skeleton as defined in claim 1 of the present application. Specifically, the presenegenin skeleton of claim 1 of the present application has carboxyl groups at positions 23 and 28, whereas the quillaic acid skeleton reviewed in Kensil reference has an aldehyde group at position 23 (corresponding to position 4 of the representative structure in Figure 6 of Kensil reference) and a carboxyl group at position 28. Furthermore, the presenegenin skeleton of the present invention

has three hydroxyl groups at positions 2, 3 and 27, whereas the quillalic acid skeleton has only two hydroxyl groups at positions 3 and 16 (different position from that of the presenegenin skeleton) (See, Figure 6 on page 41 of Kensil reference, and also page 7, lines 11 to 17 of the present application).

Therefore, Kensil reference neither discloses nor suggests saponin compounds having a presenegenin skeleton of claims 1 to 6. In addition, Kensil neither describes nor suggests an adjuvant function or induction activity of immune response of the saponin compounds having a presenegenin skeleton of the present inventions.

Furthermore, the Kensil reference teaches away from the present invention. Indeed, Kensil provides the following description (page 42, lines 1-15):

> "The fatty acid domain may play a critical role in immune stimulation. [....] Another critical group is the aldehyde at position 4 of the quillalic acid. This aldehyde is present in the major adjuvant-active saponins QS-7, QS-17, QS-18, and QS-21 (Kensil unpublished). The C4 aldehyde of QS-21 was blocked with small molecules (ethylamine, ethylenediamine, or glycine) to prevent aldehyde reactivity. These derivatives were inactive as adjuvants for either stimulation of antibody or CTL response."

(Emphasis added).

The position 4 of the quillalic acid as defined in the above passage in Kensil corresponds to a position 23 of the representative structure as shown in claim 4 of the present application. Based on the above teaching of Kensil, a person having ordinary skill in the art would not be motivated to apply a saponin compound which does not have an aldehyde group at position 4 (corresponding to position 23 of the structure formula of claim 4 of the present application) like the presenegenin skeleton saponins having a carboxyl group at that position.

Accordingly, even if Sakuma et al. (Sakuma II and I) and Kensil references are combined, the combination fails to disclose every limitation of claim 1 to 6, to the contrary, the Kensil reference teaches away from the present inventions defined in claims 1 to 6 as discussed above, thus making claim 1 to 6 non-obvious over the combination of the two references. Each of claims 7-9 depends on claim 1 and is considered patentable at least for the same reasons. Withdrawal of the rejection and reconsideration are respectfully requested.

I. Request for Rejoinder.

Claims 1-9 and 16 are directed to a composition of matter, and claims 10-15 are directed to methods of using this composition. As provided by MPEP 821.04, process claims depending from, otherwise including all the limitations of the patentable product should be entered as a matter of right if the amendment is prepared prior to final rejection or allowance.

As discussed above, claims 1-9 are considered allowable, and claims 10-15 include all the limitations of the patentable product claimed in claims 1-9. The Applicants presented the withdrawn claims 10-14 in the "withdrawn-currently amended" form as per 37 CFR 1.121(c)(2) prior to final rejection or allowance. Claim 15 remains withdrawn but should be treated for the purposes of rejoinder in the same way as claim 10, from which claim 15 depends. Accordingly, the Applicants respectfully request that claims 10-15 be rejoined at this time.

CONCLUSION

Enclosed is Check No. 576575 totaling $405.00 to cover Two Month Extension of Time fee ($225.00) and Information Disclosure Statement Fee ($180.00). The Commissioner is hereby authorized to charge any additional fees associated with the filings submitted herewith, or credit any overpayment to Deposit Account No. 07-1896.

Respectfully submitted,

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